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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/723,923	11/25/2003	Qing Wang	ROGO 217 (10309708)	9786

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EXAMINER	
DO, PENSEE T	

ART UNIT	PAPER NUMBER
1641	

DATE MAILED: 10/19/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/723,923	WANG ET AL.	
	Examiner	Art Unit	
	Pensee T. Do	1641	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *28 July 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *10-14 and 18* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *10-14 and 18* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

Detailed Action

Response to Amendment

Applicant's request for reconsideration of the finality of the rejection of the last Office action is persuasive and, therefore, the finality of that action is withdrawn.

Amendment Entry & Claim Status

The after-final amendment filed on July 28, 2005 has been acknowledged and entered.

Claims 10-14, and 18 are pending.

Withdrawn Rejection(s)

Objection to the Specification in the previous office action is withdrawn herein.

Rejection under 112, 2nd paragraph is withdrawn herein.

Rejection under 102(b) by Pope is withdrawn herein.

Rejection under 103 by Pope and Armstrong for claim 12 is withdrawn.

Rejection under 103 by Pope and Armstrong and Molna-Kimber is withdrawn for claim 13.

Maintained Rejection(s)

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 10 and 18 are rejected under 35 U.S.C. 102(b) as being anticipated by Bieniarz et al.(US 5,063,109).

Bieniarz teaches a method of attaching a ligand to a solid phase comprising contacting an amine microparticles with 2-iminothiolane HCl (a molecule which reacts with amine); reacting a conjugate comprising maleimide derivatized antibodies (linker-ligand) with said iminothiolane HCL-solid phase to attach the ligand to the microparticles. (see examples 7 & 16, especially col. 13, lines 33-40). Regarding the limitation of the molecule contains a protected or unprotected sulfhydryl group: since Bieniarz teaches the same molecule as of the present invention, such molecule must contain a protected or unprotected sulfhydryl group and must also react with the amine group in an acylation reaction. Since aminothiolane is known in the art as a Traut's reagent (see Calias 6,749,865) and iminothiolane is described in the present specification as a Traut's reagent, both must be the same and used interchangeably. Bieniarz also teaches that 2-iminothiolane-HCl is contacted to said surface of the solid phase (particle) in a solution consisting of dimethyl formamide (DMF). In example 16, the particles are treated with 2-imithiolane-HCl and then are mixed with a volume of compound 3 solution in DMF. (see examples 7 and 16).

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claim 14 is rejected under 35 U.S.C. 103(a) as being unpatentable over Bieniarz in view of Hansen et al. (US 6,663,861).

Bieniarz has been discussed above.

However, Bieniarz fails to teach a linker as p-maleimidophenyl isocyanate and contacting the surface with a 2-aminothiolane HCl, followed by contacting a sulfhydryl group provided by 2-aminothiolane-HCl with p-maleimido phenyl isocyanate.

Hansen teaches various methods of covalent coupling such as coupling a molecule with sulfhydryl groups to hydroxyl groups by using a N-(p-maleimidophenyl) isocyanate. (see col. 5, lines 15-25).

It would have been obvious to one of ordinary skills in the art to use N-(p-maleimidophenyl) isocyanate as a linker as suggested by Hansen to link the ligand which contains a hydroxyl group to 2-iminothiolane-HCl also known as 2-aminothiolane-HCl or Traut's reagent, which contains a sulfhydryl group as taught in the method of Bieniarz since Bieniarz teaches using a maleimide for linking the ligand which contains a hydroxyl group and a sulfhydryl group. N-(p-maleimidophenyl) isocyanate is known as a heterobifunctional crosslinker which links a ligand to a solid surface.

Claim 11 is rejected under 35 U.S.C. 103(a) as being unpatentable over Bieniarz (US 5,063,109) in view of Siiman et al. (US 5,639,620).

Bieniarz has been discussed above.

However, Bieniarz fails to teach magnetic particles being the solid phase.

Siiman teaches magnetic particles coated with aminodextran or gelatin which contains an amine pendent group. Crosslink the ligand/protein/antibody with the

magnetic particles by using the bifunctional crosslinking agent such as p-iminothiolane hydrochloride. The coupling of the biological substance to the particle involves activation of the free amino groups of the gelatin-coated particles with water soluble heterobifunctional reagent such as 2-iminothiolane hydrochloride (IT) also known as 2-aminothiolane-HCl or Traut's reagent, sulfosuccinimidyl-4-(N-maleimidomethyl)cyclohexane-1-carboxylate (sulfo-SMCC), m-maleimidobenzoyl-N-hydroxysuccinimide ester, N-succinimidy1-3-(2-pyridyldithio)propionate, succinimidyl-4-(p-maleimidophenyl)butyrate, N-succinimidyl-(4-iodoacetyl)aminobenzoate, the reagents listed above as substitutes for glutaraldehyde and the like. The 2-iminothiolane hydrochloride also known as 2-aminothiolane-HCl or Traut's reagent and the maleimidyl/succinimidyl reagents are preferred. (see col. 7, lines 60-65; col. 10, lines 15-25, 53-60)

It would have been obvious to one of ordinary skills in the art to use magnetic particles as a solid phase as taught by Siiman in the method of Bieniarz since both references teach a method of conjugating a ligand to a solid surface via a bifunctional crosslinking agent and because ligand bound magnetic particles, in an immunoassay, can be separated by magnetic force rather than centrifugation which is time consuming.

New Grounds of Rejection

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the

invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claim 12 is rejected under 35 U.S.C. 103(a) as being unpatentable over Bieniarz in view of Armstrong (US 5,964,996).

Bieniarz teaches a method of attaching a ligand to a solid phase comprising contacting an amine microparticles with 2-iminothiolane HCl (a molecule which reacts with amine); reacting a conjugate comprising maleimide derivatized antibodies (linker-ligand) with said iminothiolane HCL-solid phase to attach the ligand to the microparticles. (see examples 7 & 16, especially col. 13, lines 33-40). Regarding the limitation of the molecule contains a protected or unprotected sulfhydryl group: since Bieniarz teaches the same molecule as of the present invention, such molecule must contain a protected or unprotected sulfhydryl group and must also react with the amine group in an acylation reaction. Since aminothiolane is known in the art as a Traut's reagent (see Calias 6,749,865) and iminothiolane is described in the present specification as a Traut's reagent, both must be the same and used interchangeably. Bieniarz also teaches that 2-iminothiolane-HCl is contacted to said surface of the solid phase (particle) in a solution consisting of dimethyl formamide (DMF). In example 16, the particles are treated with 2-imithiolane-HCl and then are mixed with a volume of compound 3 solution in DMF. (see examples 7 and 16).

However, Bieniarz fails to teach the ligand is an antibiotic

Armstrong teaches macrocyclic antibiotic chemically bonded to a solid support such as silica gel, agarose, dextran, cellulose, branch amylose (see col. 6, lines 58-67;

col. 7, lines 5-10) via linkages such as amine, amide, thioler groups (see col. 7, lines 27-30).

It would have been obvious to one of ordinary skills in the art to attach antibiotic taught by Armstrong to solid phase according to the method of Bieniarz through routine experimentation since these antibiotics also contain a carboxyl or thiolether groups thereby enabling the reaction with a coupling agent or thiol introducing agent since both references teaching using an thioler group or amine group on a solid phase for the purpose of surface modification for attaching a ligand.

Claim 13 is rejected under 35 U.S.C. 103(a) as being unpatentable over Bieniarz et al. (US 5,063,109) in view of Armstrong (US 5,964,996) further in view of Molna-Kimber et al. (US Patent Application Publication 2002/0151088A1).

Bieniarz and Armstrong have been discussed above.

Both Bieniarz and Armstrong fail to teach antibiotic such as Rapamycin.

Molna-Kimber teaches rapamycin is a macrocylic antibiotic. (see page 1, 1st col. 2nd paragraph).

It would have been obvious to one of ordinary skills to use Rapamycin as taught by Molna-Kimber in the combination method of Bieniarz and Armstrong since Rapamycin is a macrocyclic antibiotic and Bieniarz in combination with Armstrong suggested that macrocylic antibiotics can be coupled to a solid phase for detecting specific antibodies against antibiotics. Rapamycin have immunosuppressant activity as well as antibiotic and other pharmacological activities and are useful in treating graft

and transplant rejections, diseases of inflammation and autoimmune diseases such as rheumatoid arthritis, diabetes, and multiple sclerosis.

Response to Arguments

Applicant's arguments filed July 28, 2005 have been fully considered but they are not persuasive.

Applicants amended claim 10 to incorporate the limitation of claim 17 and argue that Bieniarz fails to teach the attachment of iminothiolane in a solution of DMF. Example 16 of Bieniarz states that the antibody containing complex is introduced in DMF, but not iminothiolane.

Part (a) of example 16 is a preparation of thiolated microparticles by using pretreated amine microparticles from example 7, part a (1ml; 2.5% solids) mixed with iminothiolane HCl to achieve a final iminothiolane concentration of 50 mM. The reaction is stirred and then treated as describe in part (b) of example 7. Part (b) of example 7 requires that the amine particles to be mixed with compound 3 solution in DMF. Compound 3 according to Bieniarz is a linker. (see col. 4, lines 22-23). Then the antibody is added. Although the DMF solution is added after the iminothiolane HCl is contacted with the solid phase, it still reads on the limitation of "the molecule is contacted to said surface in a solution containing of DMF" because regardless of the order in which the DMF is added, the final product still has DMF and the solid phase contacted with iminothiolane. Furthermore, the specification of the present invention or Applicants in their response fails to discuss or describe what the advantage of adding DMF during the contact of the solid phase and iminothiolane HCl over adding DMF after

the contact of solid phase and iminothiolane HCl. Adding DMF during the contact of the solid phase and iminothiolane HCl is not defined in the present specification as the novelty of the invention.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Pensee T. Do whose telephone number is 571-272-0819. The examiner can normally be reached on Monday-Friday, 7:00-3:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Long Le can be reached on 571-272-0823. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Pensee T. Do
Patent Examiner
September 2, 2005

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10/14/05